Clinicopathological Correlations in Adult Bone Marrow Biopsies: Indications, Preliminary Diagnoses, and Histopathological Outcomes in 698 Cases

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Article

Clinicopathological Correlations in Adult Bone Marrow Biopsies: Indications, Preliminary Diagnoses, and Histopathological Outcomes in 698 Cases

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Abstract

Objective: This study aimed to analyze the demographic characteristics, clinical preliminary diagnoses, biopsy indications, and histopathological findings of adult bone marrow biopsies to construct a framework that aids clinicians and pathologists in evaluating bone marrow biopsy results. **Materials and Methods:** Bone marrow biopsy reports from 900 cases referred to the Department of Internal Diseases Hematology at Afyonkarahisar Health Sciences University from January 1, 2017, to December 31, 2021, were retrospectively analyzed. Patients with insufficient material (18) and those sent for treatment response evaluation (184) were excluded, resulting in 698 patients being included in the study. Data analysis was performed using SPSS v26, employing the McNemar test to assess clinicopathological concordance, with a significance level set at $p<0.05$. **Results:** Of the 698 patients analyzed, 388 (55.6%) were male and 310 (44.4%) were female, with ages ranging from 18 to 87 years. The most common indications for biopsy were lymphoma (16.09%), pancytopenia (16.05%), and anemia with a high sedimentation rate (14.06%). The most frequently noted preliminary diagnosis was myeloma (22.02%), followed by lymphoma (16.09%) and acute leukemia (10.03%). Significant clinicopathological concordance was observed in diagnoses such as aplastic anemia and lymphoplasmacytic lymphoma, whereas discordance was noted in conditions such as follicular lymphoma and acute myeloid leukemia (AML), reflecting the complexity and challenge of accurate diagnosis in hematologic conditions. **Conclusion:** This study documented a high incidence of lymphoma and myeloma as preliminary diagnoses, with myeloma confirmed in 52% of cases with an initial suspicion based on clinical presentation. Notable discrepancies between clinical suspicion and histopathological findings were evident in conditions such as follicular lymphoma and acute myeloid leukemia (AML), with a significant discordance rate. These findings highlight the need for enhanced diagnostic precision and the development of sophisticated diagnostic algorithms to improve the predictive accuracy of preliminary clinical diagnoses. Ultimately, this study calls for a refined approach to the clinical and pathological evaluation of bone marrow biopsies to better support therapeutic decision making and patient management.

Keywords: bone marrow biopsy; clinicopathological correlation; hematologic disease; histopathological diagnosis; diagnostic accuracy

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1. Introduction

Bone marrow examination is a fundamental diagnostic tool in medical pathology for diagnosing hematological disorders and systemic disease. Bone marrow biopsies are essential for evaluating unexplained cytopenia, diagnosing suspected hematologic malignancies, and staging known malignancies [1–3]. The diagnostic yield of bone marrow biopsies varies between 30% and 50%, with higher yields in cytopenia evaluation (49%), while cases with fever of unknown origin show lower yields, as reported by Martellosio et al. (32.7%[3]. Bone marrow biopsy is critical for lymphoma staging, as bone marrow involvement frequently occurs in lymphoma cases **[4]**. Despite advances in imaging and molecular diagnostics, bone marrow biopsy remains the gold standard for confirming clinical suspicion or revealing unexpected pathologies, particularly when preliminary tests are inconclusive [5]. Discrepancies between clinical suspicion and histopathological findings are common, and biopsies can reveal unexpected diagnoses that alter patient management [6,7]. The clinical utility of this test extends to non-hematological conditions, including disseminated infections and metastatic diseases. Studies have shown that hematological markers can predict bone marrow metastases, and granuloma detection in biopsies significantly impacts the clinical approach to granulomatous diseases [4,8].

Understanding the patterns of biopsy indications, distribution of final pathological diagnoses, and degree of clinicopathological concordance is paramount. These elements are crucial not only for refining biopsy utilization but also for enhancing the diagnostic algorithms that guide therapeutic decisions.

In this study, we performed a retrospective analysis of 698 adult bone marrow biopsies to delineate the correlation between clinical indications and preliminary diagnoses with the observed histopathological outcomes. This analysis aimed to highlight trends, pinpoint diagnostic challenges, and suggest areas for improving the indications and interpretation of biopsies. This study also aimed to contribute to the understanding of the role of bone marrow biopsy in modern medicine by providing insights into its diagnostic utility, challenges in clinical concordance, and implications for patient management across various diseases.

2. Materials and Methods

2.1. Study Design and Setting

This retrospective cohort study was conducted in the Medical Pathology Department of Afyonkarahisar Health Sciences University. We analyzed bone marrow biopsy specimens obtainedd from adult patients referredtoy the Internal Medicine Hematology unit between January 1, 2017, and December 31, 2021. This study aimed to assess the correlation between the clinical indications, preliminary diagnoses, and histopathological findings of these biopsies.

2.2. Participants

The initial cohort comprised 900 adult patients (aged ≥18 years) scheduled for diagnostic bone marrow biopsies. We excluded 18 cases due to insufficient biopsy material and 184 cases that were follow-up assessments of the treatment response. Ultimately, 698 unique diagnostic cases were included for detailed analysis, focusing on patients who underwent their first diagnostic biopsy during the study period.

Data Collection and Variables

Comprehensive data extraction involved reviewing patient demographics (age and sex), detailed clinical indications for biopsy, and preliminary diagnoses provided by referring hematologists. We categorized the biopsy indications based on clinical documentation, including symptoms such as anemia, thrombocytopenia, leukopenia, and specific clinical suspicions such as malignancies.

Each bone marrow biopsy was systematically evaluated to document the following:

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Marrow Cellularity: Classified as normocellular, hypercellular, or hypocellular relative to the patient's age.

The pathological findings included neoplastic infiltration, metastasis, granulomas, fibrosis, and other abnormalities.

Final Histopathological Diagnosis: Determined based on standard morphological assessment using hematoxylin and eosin staining and corroborated by additional findings from special staining and immunohistochemical analysis.

2.3. Histopathological Techniques

The specimens were fixed in formalin, decalcified with %10 formic acid decalcification solution for 6-8 hours, and embedded in paraffin. sections (2-3 microns) were cut and stained with hematoxylin and eosin for routine examination. Reticulin staining was performed when fibrosis assessment was necessary using a contrast-enhanced reticulin kit and graded according to the European Consensus on grading bone marrow fibrosis. Histochemical analysis was performed between 0 and 3. Bone marrow aspiration biopsy specimens were stained with Giemsa and evaluated.

2.4. Immunohistochemical Analysis

Immunohistochemical staining was tailored to the suspected clinical diagnoses using a Leica Bondmax automated system. A comprehensive panel of markers was employed based on preliminary clinical suspicion, including but not limited to CD34, CD117, TdT, MPO, CD19, CD3, and various lineage-specific markers. Staining protocols were strictly followed according to the manufacturer's guidelines, with appropriate positive and negative controls for each antibody to ensure the specificity and sensitivity of the diagnostic procedure.

2.5. Ethical Considerations

This study was approved by the local ethics committee and conformed to the ethical guidelines of the 1975 Declaration of Helsinki. Owing to its retrospective nature, patient consent was waived, and all patient data were anonymized and handled with strict confidentiality to protect patient privacy and the integrity of the data. Before starting the study, permission was obtained from the Ethics Committee of Non-Interventional Scientific Research of Afyonkarahisar Health Sciences University of the Republic of Turkey (2022/71).

2.6. Statistical Methods

Descriptive statistics were used to summarize the demographic characteristics, clinical indications, and biopsy findings. The McNemar test was used to evaluate clinicopathological concordance between the preliminary diagnoses and final histopathological outcomes, with p-values >0.05 considered indicative of significant concordance. Data were analyzed using SPSS v26 software.

3. Results

In total, 698 patients were included in this study, comprising 310 females (44.4%) and 388 males (55.6%). The age range was 18–87 years, with a median age of 64 years and a mean age of 60.29 years (SD ± 15.5). The age distribution was similar between sexes, with males having a median age of 64 years and a mean age of 60.33 (SD ± 15.51) years, and females having a median age of 63 years and a mean age of 60.24 (SD ± 15.61). Lymphoma was the most common indication for bone marrow biopsy, accounting for 16.09% of all cases, and was slightly more prevalent in males (17.05%) than in females (16.01%). Pancytopenia followed closely, representing 16.05% of the cases, with a higher occurrence in females (20.0%) than in males (13.07%). Anemia with a high rate comprised 14.06% of the indications, more commonly in males (16.0%) than in females (12.09%) (Table 1).

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Table 1. Gender-Specific Distribution of Bone Marrow Biopsy Indications.

Indication	Total (n)	Total (%)	Male (n)	Male (%)	Female (n)	Female (%)
Lymphoma	118	16.09	68	17.05	50	16.01
Pancytopenia	115	16.05	53	13.07	62	20.0
Anemia with High Sed Rate	102	14.06	62	16.0	40	12.09
Cytopenia	85	12.02	52	13.04	33	10.06
Thrombocytosis	77	11.0	43	1101	34	11.0
Leukocytosis	57	8.02	32	8.02	25	8.01
Bicytopenia	55	7.09l	21	5.04	34	11.0
Solid Tumor	26	3.07	14	3.06	12	3.09
Plasmacytoma/Myeloma	22	3.02	15	3.09	7	2.03
MDS	21	3.0	13	3.04	8	2.06
Lymphocytosis	7	1.0	5	1.03	2	0.6
Other*	13	1.09	10	2.07	3	1.0
Total	**698**	**100.0**	**388**	**100.0**	**310**	**100.0**

*unexplained fever, monocytosis, lymphadenopathy, refractory ITP, mastocytosis, eosinophilia, non-amyloidosis-related renal biopsy, sarcoidosis, prolonged acute renal failure. MDS: Myelodysplastic Syndrome.

The distribution of preliminary diagnoses from bone marrow biopsies was analyzed. Myeloma was the most common preliminary diagnosis and was identified in 155 patients (22.02%), with a higher prevalence in males (24.0%) than in females (20.0%). Lymphoma Staging was the second most common reason for biopsy in 118 patients (16.09%). Males again showed a slightly higher percentage (17.05%) than females (16.01%). Acute Leukemia and MDS were also notable diagnoses that led to biopsy, with acute leukemia present in 72 patients (10.03%) and MDS in 71 patients (10.02%). No preliminary diagnosis was noted in 68 patients (9.07%), with a slightly higher incidence in females (11.09%) than in males (8.0%) (Table 2).

Table 2. Gender-Specific Distribution of Preliminary Diagnoses for Bone Marrow Biopsy.

Preliminary Diagnosis	Total (n)	Total (%)	Male (n)	Male (%)	Female (n)	Female (%)
Myeloma	155	22.02	93	24.0	62	20.0
Lymphoma Staging	118	16.09	68	17.05	50	16.01
Acute Leukemia	72	10.03	39	10.01	32	10.03
MDS	71	10.02	40	10.03	31	10.0
No Preliminary Diagnosis	68	9.07	31	8.0	37	11.09
Chronic Myeloproliferative Disorder	68	9.07	34	8.08	34	11.0
CLL/SLL	30	4.03	21	5.04	9	2.09
Chronic Myeloid Leukemia	28	4.0	15	3.09	13	4.02
Bone Marrow Involvement	25	3.07	14	3.07	12	3.09
Acute Myeloid Leukemia	21	3.0	10	2.07	11	3.05
Other*	19	2.07	11	2.08	8	2.07
ITP	7	1.0	3	0.8	4	1.03
Myelofibrosis	6	0.9	5	1.03	1	0.3

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Acute Leukemia, MDS	5	0.7	1	0.3	4	1.03
Acute Lymphocytic Leukemia	5	0.7	3	0.8	2	0.6
Total	**698**	**100.0**	**388**	**100.0**	**310**	**100.0**

*amyloidosis, aplastic anemia, additional leukemia or lymphoma types, unexplained fever, monocytosis, mastocytosis, granulomatous disease, autoimmune hemolytic anemia. CLL: Chronic Lymphocytic Leukemia , SLL: Small Lymphocytic Lymphoma , AML: Acute myeloid Leukemia , ITP: Idiopathic Thrombocytic Purpura MDS: Myelodysplastic Syndrome , ALL: Acute Lymphoblastic Leukemia.

The distribution of histopathological diagnoses following bone marrow biopsy was analyzed. Normocellular non-marrow emerged as the most prevalent finding, identified in 244 cases, accounting for 35.0% of all diagnoses, distributed between males (34.3%) and females (35.8%). Hypercellular bone marrow was diagnosed in 175 patients (25.0%). Myeloma was the third most common specific diagnosis, found in 90 cases (12.9%) of the cohort, with a higher occurrence in males (14.4%) than in females (11.0%) (Table 3).

Table 3. Gender-Specific Distribution of Diagnoses of Bone Marrow Biopsy.

Diagnosis	**Total (n)**	**Total (%)**	**Male (n)**	**Male (%)**	**Female (n)**	**Female (%)**
Normocellular Bone Marrow	244	35.0	133	34.3	111	35.8
Hypercellular Bone Marrow	175	25.0	97	25.0	78	25.02
Myeloma	90	12.09	56	14.04	34	11.0
Lymphoma	70	10.0	-	-	-	-
Acute Myeloid Leukemia	63	9.0	26	6.07	37	11.09
Acute Lymphoblastic Leukemia	16	2.03	5	1.03	11	3.05
Carcinoma Infiltration	13	1.09	7	1.08	6	1.09
Aplastic Anemia	8	1.01	5	1.03	3	1.0
Myelofibrosis	7	1.0	5	1.03	2	0.6
Hypocellular Bone Marrow	6	0.9	4	1.0	2	0.6
Granuloma	3	0.4	1	0.3	2	0.6
Mast Cell Leukemia	1	0.1	-	-	1	0.3
Increased Histiocytes in Bone Marrow	1	0.1	-	-	1	0.3
Necrosis	1	0.1	1	0.3	-	-
Total	**698**	**100.0**	**388**	**100.0**	**310**	**100.0**

Preliminary clinical diagnoses and histopathological findings were evaluated. Among the 102 patients with anemia and a high sedimentation rate, the majority were preliminarily diagnosed with multiple myeloma (92.2%) and MDS (3.9%). The pathological diagnoses confirmed multiple myeloma in 52% of these cases, 30.4% had normocellular bone marrow, and 7.8% had hypercellular bone marrow. Among the 55 patients evaluated for bicytopenia, acute leukemia was the most suspected diagnosis (21.8%), followed by MDS (16.4%), and AML (9.1%). Pathologically, 30.9% of the patients had hypercellular bone marrow, indicative of an active marrow process, 21.8% had AML, and 21.8% had normocellular bone marrow. Bone marrow involvement was suspected in 118 patients undergoing lymphoma staging and was pathologically confirmed in 72% of the patients as normocellular bone marrow. A total of 7.6% had DBBHL, and 4.2% exhibited hypercellular bone marrow (Table 4).

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Table 4. Preliminary Diagnoses and Corresponding Pathological Outcomes.

Condition	Total Patients	Preliminary Diagnoses	Confirmed Pathological Diagnoses
Anemia and High Sedimentation Rate	102	Multiple Myeloma (92.2%), MDS (3.9%)	52% Multiple Myeloma, 30.4% Normocellular BM, 7.8% Hypercellular BM
Bicytopenia	55	Acute Leukemia (21.8%), MDS (16.4%), AML (9.1%)	30.9% Hypercellular BM, 21.8% AML, 21.8% Normocellular BM
Lymphoma Staging	118	Bone Marrow Involvement (100%)	72% Normocellular BM, 7.6% DBBHL, 4.2% Hypercellular BM
Lymphocytosis	7	CLL/SLL (57.1%)	42.9% CLL/SLL, 14.3% Marginal Zone Lymphoma
Leukocytosis	57	CLL (42.1%), CML (28.1%), Acute Leukemia (15.8%)	36.8% CLL/SLL, 29.8% Hypercellular BM, 12.3% AML
MDS	21	MDS (47.6%), progression to AML (28.6%)	47.6% Hypercellular BM, 23.8% AML
Pancytopenia	115	No Preliminary Diagnosis (40.9%), Acute Leukemia (18.3%)	29.6% Hypercellular BM, 23.5% Normocellular BM, 17.4% AML
Plasmacytoma/Myeloma Follow-up	22	Multiple Myeloma (100%)	63.6% Multiple Myeloma, 27.3% Normocellular BM
Cytopenia	85	MDS (37.6%), Acute Leukemia (18.8%), Multiple Myeloma (18.8%)	34.1% Normocellular BM, 29.4% Hypercellular BM, 16.5% AML
Malignant Epithelial Tumor Follow-up	26	Bone Marrow Involvement (100%)	53.8% Normocellular BM, 19.2% Carcinoma Infiltration
Thrombocytosis	77	Chronic Myeloproliferative Disorder (77.9%)	59.7% Hypercellular BM, 28.6% Normocellular BM
Other Indications	13	Various (30.8% other reasons)	46.2% Hypercellular BM, 30.8% Normocellular BM

DBBHL: Diffuse Large B-Cell Lymphoma, CLL/SLL: Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma, CML: Chronic Myeloid Leukemia, AML: Acute Myeloid Leukemia, ALL: Acute Lymphoblastic Leukemia, MDS: Myelodysplastic Syndrome, ITP: Idiopathic Thrombocytopenic Purpura.

The concordance between preliminary clinical diagnoses and histopathological findings in 698 bone marrow biopsy cases was evaluated. Six diagnoses matched well between the clinical expectations and histopathological confirmation, showing no significant statistical discrepancies ($p > 0.05$): aplastic anemia, lymphoplasmacytic lymphoma, CLL/SLL, mantle cell lymphoma, marginal zone lymphoma, and myelofibrosis. Seven diagnoses were significantly discordant ($P \leq 0.05$): carcinoma infiltration, follicular lymphoma, AML, ALL, diffuse large B-cell lymphoma, Hodgkin lymphoma, and multiple myeloma (Table 5).

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Table 5. Concordance Analyses of Clinical Preliminary Diagnoses, Histopathological Findings, and Indications.

Diagnosis	Concordance	p	Indications (Number of Patients)	% of Total Indications
Aplastic Anemia	Concordant	0.13	Pancytopenia (5), Anemia and High Sed Rate (1), Bicytopenia (1), Cytopenia (1)	62.5%, 12.5%, 12.5%, 12.5%
Lymphoplasmacytic Lymphoma	Concordant	1.0	Anemia and High Sed Rate (1), Pancytopenia (1), Other (Sarcoidosis) (1)	33.3% each
CLL/SLL	Concordant	0.29	Lymphocytosis (4)	57.1%
Mantle Cell Lymphoma	Concordant	0.69	Lymphoma Staging (4)	3.4%
Marginal Zone Lymphoma	Concordant	1.0	Anemia and High Sed Rate (1), Pancytopenia (1), Other (Sarcoidosis) (1)	33.3% each
Myelofibrosis	Concordant	1.0	Thrombocytosis (3), Cytopenia (3), Leukocytosis (1)	42.9%, 42.9%, 14.3%
Carcinoma Infiltration	Discordant	0.04	Solid Tumor (5), Bicytopenia (4), Pancytopenia (2), Anemia and High Sed Rate (1), Lymphoma (1)	38.5%, 30.8%, 15.4%, 7.7%, 7.7%
Follicular Lymphoma	Discordant	0.02	Lymphoma Staging (3), Lymphocytosis (3), Pancytopenia (4), Cytopenia (3)	5.7%, 5.7%, 7.1%, 4.3%
AML	Discordant	0.00	Bicytopenia (12), Pancytopenia (20), Other (2)	21.8%, 17.4%, 1.7%
ALL	Discordant	0.00	Pancytopenia (8), Bicytopenia (3), Thrombocytosis (2), Lymphoma (1), Lymphocytosis (1), Leukocytosis (1)	50%, 18.8%, 12.5%, 6.3%, 6.3%, 6.3%
Diffuse Large B-cell Lymphoma	Discordant	0.00	Lymphoma Staging (9)	7.6%
Hodgkin Lymphoma	Discordant	0.00	Lymphoma Staging (3), Leukocytosis (22)	2.5%, 31.4%
Multiple Myeloma	Discordant	0.00	Multiple Myeloma (14)	63.6%

McNemar test.

4. Discussion

Bone marrow biopsy is essential for diagnosing hematologic and systemic diseases. Studies show its diagnostic yield varies by clinical context, from 30% to 50%. Martellosio et al. reported a yield of 32.7%[3]. The yield varies by indication: cytopenias have high yields (49%), while fever of unknown origin yields only 5–6% when isolated [3]. This shows bone marrow biopsy is most accurate with hematologic abnormalities and limited in systemic presentations. Our retrospective study of 698 specimens showed similar results, with specific pathologies identified in many cases, aligning with the 30–50% range in literature[1,3,5]. Diagnostic success was highest for cytopenia-related indications and lowest for systemic inflammatory syndromes. Noiperm et al. found yields of 27–54% in HIV-

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positive patients with FUO when opportunistic infections or hematologic malignancies were present[9]. These data show biopsy accuracy is context-dependent, excelling in hematologic disorders but less in systemic symptoms. The literature confirms bone marrow examination provides critical diagnostic information, though not all biopsies are diagnostic. The high specificity of bone marrow histopathology indicates abnormal findings usually indicate disease, particularly in cases of lymphoma or metastatic carcinoma, where positive biopsies confirm advanced disease.

The data reveal diverse indications for bone marrow biopsy across sexes. Leading indications include lymphoma, pancytopenia, and anemia with high sedimentation rates. Pancytopenia was more prevalent in females (20.0%) than males (13.07%), suggesting gender-related variations in pathophysiology that warrant investigation. The consistency with findings by Bhuyan et al. highlights the diagnostic reliability across different settings[1]. Understanding these distributions is crucial for refining diagnostic strategies and developing gender-specific algorithms. Myeloma was more common in males (24.0%) than females (20.0%), aligning with literature showing male predominance[5]. Chronic myeloproliferative disorders were equally prevalent among sexes (9.07%), reflecting their nonspecific presentation requiring histopathological confirmation, as emphasized by Ng et al.[10]. A significant proportion of cases lacking preliminary diagnosis revealed severe hematological conditions, indicating the need for refined assessment tools. The distribution showed higher incidence of myeloma and AML in males than females, correlating with sex-related differences in hematological malignancies[5]. The higher prevalence of AML in females (11.09%) than males (6.07%) suggests need for increased surveillance. Multiple myeloma was confirmed in 52% of initially suspected cases, while discrepancies occurred in bicytopenia cases, where suspected acute leukemia was confirmed as AML in only 21.8% of cases.

Statistical analyses of bone marrow biopsy data have been used to quantify concordance and identify predictive factors. This study aimed to identify clinical findings that correlate with biopsy outcomes, guiding evidence-based use of marrow biopsies. The study compared clinical and pathological diagnoses, finding no significant difference in six diagnostic categories and significant differences in seven others. Diagnoses of aplastic anemia or chronic lymphoproliferative disorders usually match the expected marrow findings due to distinctive features. However, significant discordance was found in acute leukemia or multiple myeloma, where the marrow often did not confirm clinical suspicion. Multiple myeloma was a common preliminary diagnosis (22% of cases), but only half had pathologically proven myeloma, with others showing reactive marrow or amyloidosis. Similarly, suspected acute leukemia cases were found to have myelodysplastic syndrome or reactive hyperplasia and vice versa. Discordances appeared in lymphoma cases, where about one-quarter of patients sent for “lymphoma staging” had unrelated or benign marrow pathology, indicating unwarranted concern for marrow involvement.

Statistical correlation studies have identified clinical predictors of positive bone marrow biopsy findings. Martellosio et al. reported that blood count abnormalities, including anemia, neutropenia, or circulating blasts, increased the odds of a diagnostic marrow biopsy. In patients with fever of unknown origin, those with cytopenia had a higher chance of diagnostic bone marrow biopsy[11]. These findings are significant; peripheral blood abnormalities reflect marrow pathology, strengthening pre-test probability. In solid tumors, Agrawal et al. found that high NLR and elevated lactate dehydrogenase (LDH) were associated with metastatic involvement. NLR above 3.5 and LDH above 450 U/L had good specificity for predicting marrow metastasis[12]. Such correlations suggest clinicians can use blood markers to determine when marrow biopsy is informative in cancer staging. Our study highlights diagnoses likely to be confirmed by biopsy. Analysis showed a significant false-positive rate for AML, indicating ancillary tests are crucial before diagnosis. Lymphoplasmacytic lymphoma shows perfect concordance in clinical and histopathological alignment, especially in sarcoidosis[3]. Discordance in AML and ALL highlights diagnostic challenges requiring comprehensive strategies, including cytogenetic and molecular analyses[1]. Significant discordance in lymphoma staging suggests complications in interpretation, emphasizing the need for advanced

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diagnostic tools[13]. Statistical analyses provide understanding of clinicopathological relationships, supporting evidence-based improvements in bone marrow examinations.

Recent studies, including ours, have significant implications for refining diagnostic algorithms and improving patient management. Recognizing diagnostic yield patterns can enhance the performance of bone marrow biopsy. Yields are highest with cytopenia or abnormal blood counts; thus, algorithms can prioritize bone marrow examination in these cases, while opting for noninvasive tests first in isolated fever or lymphadenopathy without blood abnormalities. Some authors suggest risk stratification models; for instance, in HIV-related FUO, bone marrow biopsy is performed only if criteria such as cytopenia or elevated liver enzymes are met [9]. Our data supports this approach. In cases of low diagnostic success, consider alternative pathways initially, reserving biopsy for persistently unexplained cases. Our finding that suspected multiple myeloma or leukemia can often be incorrect supports the maintenance of a broad differential diagnosis and the integration of early biopsy or confirmatory tests. Improved algorithms might include checkpoints; if a patient is labeled as having AML but the biopsy is negative for blasts, prompt evaluation for other causes, such as myelodysplasia or aplastic anemia. The goal is to realign patient management when biopsy results contradict clinical expectations, as was necessary in many of our cases.

Another key implication is integrating ancillary testing with bone marrow biopsy. Combining morphology with immunophenotyping, cytogenetics, and molecular studies enhances diagnostic accuracy and prognosis. In multiple myeloma, immunohistochemistry can identify poor prognostic markers[14–17]. Szczepaniak et al. showed that detailed histological evaluation stratified myeloma patients by risk and survival[5]. This emphasizes that marrow biopsies provide prognostic information for patient management. Cases where biopsy revealed unexpected high-risk pathology led to significant therapy changes. Granulomas in the marrow affect clinical approach, prompting infectious workups or immunosuppressive therapy, and new methods have been proposed for diagnosing granulomatous lesions[8]. These innovations could improve examination yield and ensure timely treatment. Standardization of marrow biopsies is crucial. Due to variability in performing and reporting biopsies, harmonized pathology criteria are needed. Ng et al. found that reporting variability led to MPN subtype misclassification[10]. Incorporating decision support tools and AI analysis can enhance diagnostics[9,18–20]. When clinical expectations and pathologies differ, interdisciplinary reviews can update diagnostic algorithms. Evidence-based insights have improved diagnostic pathways, leading to a tailored approach: performing appropriate biopsies and using results to guide therapy. Our findings support refined algorithms that maximize diagnostic yield while minimizing unnecessary procedures for better patient care.

Study Limitations

Despite these comprehensive findings, this study had several limitations that should be considered. The retrospective design of the study inherently limits its ability to control for confounding variables and biases that may influence outcomes. This includes potential selection bias, as the cases were based on available records, which might not represent all demographic or clinical scenarios. The findings are based on data from a single medical institution, which may not be generalizable to other settings owing to variations in demographic characteristics, clinical practices, or healthcare delivery systems.

5. Conclusions

The study revealed patterns in diagnostic accuracy across hematological conditions, with lymphoma and myeloma being the most common preliminary diagnoses. While myeloma was confirmed in 52% of cases initially suspected based on clinical presentations, notable discordance was observed in conditions like follicular lymphoma and AML, where clinical hypotheses often did not align with histopathological outcomes. This research identifies a need for enhancing diagnostic precision, particularly in myeloma and AML interpretation, where high discordance could impact clinical decision-making. The study demonstrates the importance of comprehensive

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clinicopathological evaluation to improve predictive accuracy of preliminary clinical assessments, refining therapeutic strategies and patient management. Analysis quantified concordances and discordances in preliminary and final diagnoses, highlighting challenges in bone marrow diagnostics. These findings advocate for better integration of clinical data with histopathological insights to optimize the diagnostic protocols and treatment pathways for hematological malignancies.

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